Case Report

Synchronous multifocal osteosarcoma with small cell histological variant: A double rarity

Sonia Gon, Tamalika Kundu, Bidisha Naskar Ghosh[1]

Department of Pathology, ESI-PGIMSR and ESIC Medical College, [1]Department of Radiotherapy, Institute of Post Graduate Medical Education and Research, Kolkata, West Bengal, India

ABSTRACT

Multifocal osteosarcoma (MFOS), osteosarcoma involving multiple sites, is a rare variant of osteosarcoma. When the lesions appear within 6 months of initial presentation of the tumor, it is known as synchronous MFOS. Synchronous MFOS has an incidence of 1%–3% only. Moreover, the histological variant of small cell osteosarcoma is even rarer. A case of 14-year-old male with synchronous MFOS of small cell type involving frontal and mandibular bone simultaneously is being reported here. It poses a dilemma to both the clinician and the pathologist to diagnose whether it represents multiple primary tumor or metastatic disease.

Key words: Multifocal, osteosarcoma, small cell, synchronous

INTRODUCTION

Osteosarcoma is a highly malignant bone tumor mainly involving a single location in the metaphysis of long bones.[1] However, it may rarely involve more than one bone at the time of initial examination, and if there is no pulmonary metastasis, it is known as multicentric or multifocal osteosarcoma (MFOS). The incidence of MFOS is 1%–2% of all osteosarcoma, and it may present as a synchronous or metachronous tumor.[2] When multiple lesions appear within 6 months of initial presentation of the tumor, it is known as synchronous MFOS, and multiple lesions presenting after 6 months are called as metachronous MFOS.

Synchronous MFOS is a rare condition, with a reported incidence of 1%–3% and the histological variant of small cell osteosarcoma is even rarer.[3] It poses a diagnostic dilemma both for the clinician and the pathologist as the question "whether it represents multiple primary tumor or metastatic disease," is still a matter of debate.[4] A case of 14-year-old male with synchronous MFOS involving frontal and mandibular bone simultaneously is being reported here with an interesting and even rarer histological variant of small cell osteosarcoma.

CASE REPORT

A 14-year-old male patient presented in the outpatient Department of Plastic and Reconstructive Surgery with rapidly growing swelling over the left side of mandible since 3 months. The swelling was tender and had involved the medial half of the mandible on the left side, measuring 9.5 cm × 4 cm. There was a scar mark on the scalp at the region of frontal bone.

Patient had a past history of rapidly growing swelling over forehead and angle of mandible left side since 8 months. Initially, the swelling had started at the frontal region and within 1 month another swelling occurred at the mandibular region. There was no history of trauma or exposure to the radiation. There was no significant past history apart from

Address for correspondence: Dr. Tamalika Kundu, Flat No. B2, Niva Park Phase 5, Kolkata - 700 096, West Bengal, India.
E-mail: drtamakunduray@gmail.com

Access this article online

Quick Response Code:

Website: www.ccij-online.org

DOI: 10.4103/2278-0513.200111

Cite this article as: Gon S, Kundu T, Ghosh BN. Synchronous multifocal osteosarcoma with small cell histological variant: A double rarity. Clin Cancer Investig J 2016;5:533-6.

the history of mumps 3 years back. Patient was subjected to fine-needle aspiration cytology from both the frontal and mandibular swelling which revealed discrete small round cell exhibiting minimal nuclear and cellular pleomorphism favoring a cytomorphological diagnosis of Ewing's sarcoma or primitive neuroectodermal tumor [Figure 1].

Contrast-enhanced computed tomography (CT) scan of head and neck region showed the presence of calvarial lesion in left frontal bone with spicule-like new bone formation along with widening, bone erosion, and destruction at anterior cortex of left half of the body of mandible, suggesting a diagnosis of primary bone-forming tumor [Figure 2]. Incisional biopsy was done from the frontal as well as mandibular swelling, and the specimen was sent to the Department of Pathology for histopathological examination for exact categorization of the tumor. Microscopic examination revealed a tumor composed of malignant small round cells with moderate mitotic activity and focal osteoid formation [Figure 3]. Tumor cells on immunohistochemistry expressed vimentin, osteonectin, and synaptophysin but were negative for cytokeratin, desmin, and leukocyte common antigen. Histopathological diagnosis of small cell variant of osteogenic sarcoma was preferred over Ewing's sarcoma based on microscopic and immunohistochemical characteristics of tumor cells.

Subsequently, the patient underwent chemotherapy with cyclophosphamide and doxorubicin over a period of 15 weeks. Both the swellings dramatically reduced in size. Removal of frontal bone was done afterward, and the biopsy confirmed the absence of any neoplastic process. However, patient again presented with trismus and a mass at retromolar region encroaching in adjoining cheek 3 months after the initial chemotherapy. Patient was given radiation for the same followed by six cycles of chemotherapy, with almost complete disappearance of the swelling.

After a gap of 6 months of disease-free interval, patient has now presented with recurrence of the swelling involving left half of the body of mandible and ramus. On local examination, the swelling is tender and measures 9.5 cm in its greatest dimensions and involves left side of the mandible. CT scan has revealed punched-out bone erosion in the medial aspect of ramus and anterior cortex of left half of the body of the mandible with enhancing periosseous soft tissue mass measuring 31 mm × 13 mm. The frontal bone is unremarkable. Unfortunately, patient died after 2 days due to cardiorespiratory failure.

DISCUSSION

Origin of synchronous MFOS is debatable whether it represents multiple primary tumor or metastatic disease. As hematogenous spread is the main metastatic route, if pulmonary metastasis is not present, it is thought to be a multiple primary tumor. Moreover, cases related to p53

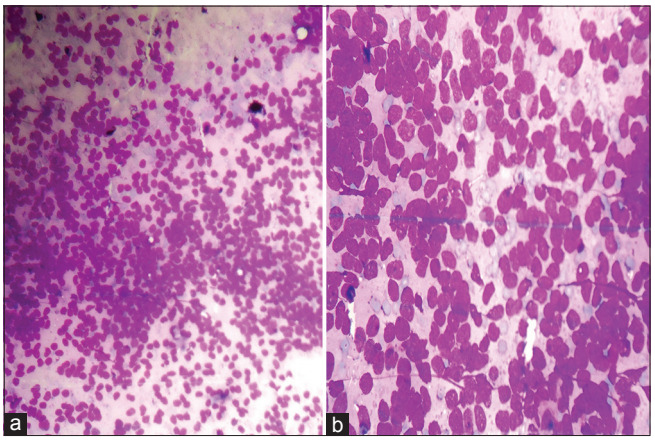

Figure 1: May–Grunwald Giemsa-stained fine-needle aspiration cytology smears from both the lesions showing discrete small round cells in low power (a) and high power (b) view exhibiting minimal pleomorphism

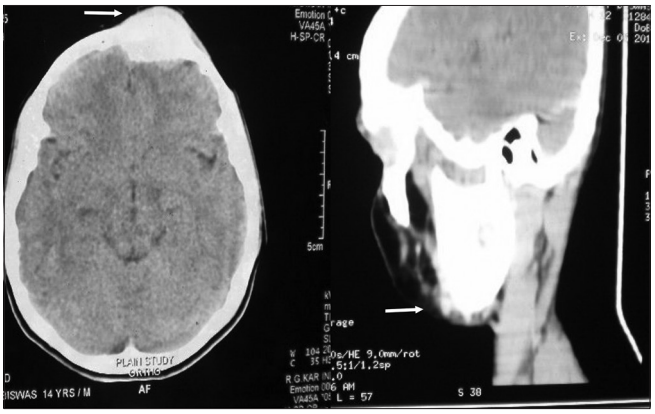

Figure 2: Contrast-enhanced computed tomography scan of head and neck region showing the presence of calvarial lesion in left frontal bone with new bone formation and widening, bone erosion, and destruction at anterior cortex of left half of the body of mandible

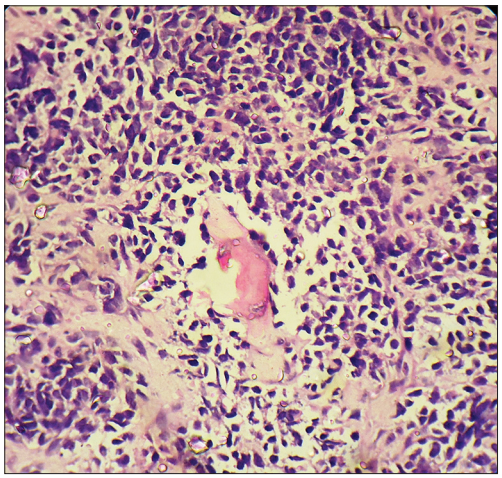

Figure 3: H- and E-stained sections showing a tumor composed of malignant small round cells with moderate mitotic activity and focal osteoid formation

mutation and retinoblastoma suggest a possible mechanism for multiple primary tumors over metastatic theory.[4] However, if large dominant lesion is found at the time of presentation, metastatic theory is more favored. This can be explained by bone-to-bone metastasis as seen in prostate cancer through Batson's venous plexus or intraosseous embolization through marrow sinusoids.[5,6] Metastasis can also occur through lymphatic spread.[3] The present case had two lesions at a different site which arose within 1 month of each other with none of the lesions representing a dominant one and with no evidence of pulmonary or any other metastasis, leading the authors to believe it to be more of multiple origins of primary tumor. Small cell variant of osteosarcoma on histopathology was another interesting and unusual finding found in the present case, which makes the case even rarer.

Small cell osteosarcoma is an exceedingly rare tumor, estimated to account for <1% of all cases of osteosarcoma.[7] It presents with age, anatomic distribution, radiological, and cytological picture similar to conventional osteosarcoma except macronucleoli, prominent spindled morphologic features, plasmacytoid morphologic features, cellular necrosis, and relatively abundant osteoid. Hence, differentiating it from other small round cell tumors of the bone such as Ewing's sarcoma, mesenchymal chondrosarcoma, non-Hodgkin lymphomas, and metastatic neuroblastoma is a challenge both for the clinician and the pathologist.[7-9]

The presence of osteoid is a prerequisite for differentiating small cell osteosarcoma from Ewing's sarcoma. The problem arises when fibrin presents between the tumor cells in Ewing's sarcoma resembles lacy osteoid of small cell osteosarcoma, but it is never mineralized.

The presence of both cartilage and osteoid again favors a diagnosis of small cell osteosarcoma rather than mesenchymal chondrosarcoma as latter do not show osteoid formation. Moreover, typical "staghorn," hemangiopericytoma-like vessels generally not seen in small cell osteosarcoma. The cells of malignant lymphoma generally have larger nuclei, often with vesicular chromatin, irregular nuclear membranes, prominent nucleoli, a lack of cellular cohesion, and lymphoglandular bodies. Neuroblastoma metastatic to bone may also mimic small cell osteosarcoma. The presence of Homer Wright rosettes or pseudorosettes supports a diagnosis of neuroblastoma over small cell osteosarcoma.[7,9] Immunohistochemically, the tumor cells in small cell osteosarcoma are positive for many markers such as cytokeratin, smooth muscle actin (SMA), vimentin, osteonectin, and osteocalcin. CD99 which is considered a specific marker for Ewing's sarcoma may be positive in small cell osteosarcoma, but they are consistently negative for leukocyte common antigen (LCA), B- and T-cell markers specific for lymphoma/leukemia. A diagnosis of small cell variant of osteosarcoma was made in the present case keeping in mind the presence of mineralized osteoid on histopathology along with tumor cell expression for variable markers such as vimentin, synaptophysin, SMA, and osteonectin and also, the negative expression of tumor cells for LCA.

The prognosis of small cell osteosarcoma was considered to be worse than conventional osteosarcoma and Ewing's sarcoma. The overall survival rate depends on prognostic factors such as tumor size, location, and histologic grade. Treatment includes aggressive local or radical excision of the tumor as wide excision of adjacent bone and periosteum not only prevents recurrence by removing small satellite lesions but also prevents the local spread of tumor along bone surface. And also, recurrent lesions are much more aggressive having a higher grade of malignancy which increases the risk of further recurrence or metastasis. Chemotherapy further helps by improving primary control and eradicating systemic disease.[10]

CONCLUSION

Exact categorization of osteosarcoma with the help of clinical, radiographic, and microscopic characteristics along with the aid of ancillary technique such as immunohistochemistry is the key to establish an effective therapeutic regimen that will improve the survival rate of the patient.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Resnick D, Kyriacos M, Greenway GD. Tumors and tumor like lesions of bone: Imaging and pathology of specific lesions. In: Resnick D, editor. Diagnosis of Bone and Joint Disorders. Philadelphia: Saunders; 1995. p. 3697-9.
2. Jones RD, Reid R, Balakrishnan G, Barrett A. Multifocal synchronous osteosarcoma: The Scottish Bone Tumour Registry experience. Med Pediatr Oncol 1993;21:111-6.
3. Hatori M, Ohtani H, Yamada N, Uzuki M, Kokubun S. Synchronous multifocal osteosarcoma with lymphatic spread in the lung: An autopsy case report. Jpn J Clin Oncol 2001;31:562-6.
4. Currall VA, Dixon JH. Synchronous multifocal osteosarcoma: Case report and literature review. Sarcoma 2006;2006:53901.
5. Enneking WF, Kagan A. "Skip" metastases in osteosarcoma. Cancer 1975;36:2192-205.
6. Batson OV. The vertebral vein system. Am J Roentgenol 1957;78:195-212

7. Unni KK, Inwards CY, Bridge JA, Kindblom LG, Wold LE. Tumors of the bones and joints. 4th series ed. AFIP Atlas of Tumor Pathology. Washington, DC: American Registry of Pathology; 2005
8. Nakajima H, Sim FH, Bond JR, Unni KK. Small cell osteosarcoma of bone. Review of 72 cases. Cancer 1997;79:2095-106.
9. Hameed M. Small round cell tumors of bone. Arch Pathol Lab Med 2007;131:192-204.
10. Sethi A, Rehani S, Kundendu A. Small cell osteosarcoma of mandible: A rare case report and review of literature. J Clin Exp Dent 2010;2:96-9.